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Aminophosphine Complex as a Catalyst Precursor in Suzuki Coupling Reactions†

Research article

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Abstract: A palladium complex with an aminophosphine ligand has been prepared and investigated as a catalyst precursor in Suzuki coupling reactions in toluene. Nanoparticles composed of elemental palladium have been isolated from the reaction media and analyzed using transmission electroscopic microscope (TEM), which shows the essential catalysts palladium nanoparticles to have a size of ca. 3.0 nm.

Keywords: *Aminophosphophosphine • Transition metal complex • X-ray • Catalysis • Nanoparticles*

1. Introduction

The chemistry of aminophosphines with direct P-N bond is a topical and challenging area in main group chemistry [1-6]. Functionalized aminophosphines with additional donor groups are particularly interesting since they can significantly modify the properties of the molecules [7-12] and thus play an important role in their applications [13,14]. Transition metal complexes of aminophosphines and phosphinoamides are valuable molecules since they can serve as catalyst in a number of organic processes [1-4]. But due to problems associated with the weakness of the P-N bond, the application of aminophosphines and their complexes is still relatively unexplored compared to the chemistry of traditional phosphines, for which their palladium complexes have found widespread interest in academic research and in industry [15].

In recent years, there is a growing interest in aminophosphine ligands, which are synthetically accessible, and are endowed with attributes that could make them more suitable ligands than traditional phosphines [1-4]. One such attribute is the electron-rich nature of aminophosphines, in comparison to phosphines. lit has been shown that a catalytic system comprising $Pd_2(dba)_3$ and semi-labile aminophosphines exhibited superior catalytic activity in C-C coupling reactions compared to those using traditional phosphines [16-19]. In particular, functionalized aminophosphines can significantly alter the properties of the transition-metal complex [3], thereby providing a strategy to enhance the activity of such catalytic systems [4].

The Suzuki reaction is an important example of C-C coupling reaction and is achieved using boronic acids and haloarenes [20], although chloroarenes are seldom employed given the poor reactivity of the C-Cl bond [21]. Despite numerous publications on Suzuki reactions in molecular solvents [22-25], and more recently in ionic liquids (IL) [26,27], one commonly accepted theory is that the Pd(0) species, formed *in situ*, is the active catalysts in such systemsn [28]. Using highly polar ionic liquids as solvent, palladium nanoparticles have been isolated and analyzed to shed light on the reaction mechanism [29-31]. In this paper we report the use of a palladium-aminophosphine complex as a pre-catalyst for Suzuki C-C coupling reactions and discuss the role of palladium nanoparticles in the catalytic system.

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† *60th birthday of Prof. Dr. Yuan Kou*

2. Experimental

All manipulations were performed under an inert atmosphere of dry nitrogen using standard Schlenk techniques using solvents dried by the appropriate reagents and distilled prior to use. Aminophosphine **1** was prepared according to previously published method. ^{14}NMR spectra were obtained at 20°C on a Bruker DMX 200 instrument using $SiMe_4$ for ^{1}H and 85% H_3PO_4 for ^{31}P as external standards. ESI-MS spectra were recorded on a ThermoFinnigan LCQ™ Deca XP Plus quadrupole ion trap instrument using a literature procedure [44]. Samples were infused directly into the source at 5 µL min^{-1} using a syringe pump. The spray voltage was set at 5 kV and the capillary temperature at 50°C. The MS detector was tuned automatically on the base peak, which optimized the remaining parameters. Elemental analysis was carried out at the Institute of Chemical Sciences and Engineering (EPFL).

2.1. Synthesis of [Pd{C_6H_4(p-CN)N(PPh_2)$_2$}Cl_2]2

$Pd(cod)Cl_2$ (14.3 mg, 0.05 mmol) in dichloromethane (5 ml) was added to a solution of **1** (30.2 mg, 0.1 mmol) in dichloromethane (5 ml) at 0°C over a period of 10 minutes. After addition was complete, the reaction mixture was allowed to warm up to room temperature. The progress of the reaction was monitored using ^{31}P NMR spectroscopy. When the reaction was complete, the solvent was removed under *vacuum* and diethyl ether (2 ml) was added, and the sample was left to stand at 2°C for 24 h. The white precipitate formed was filtered and dried *in vacuo* (23.2 mg, yield 70%). Crystals suitable for X-ray diffraction analysis were grown from a solution of dichloromethane/diethyl ether solution at -21°C. M.p. > 285°C (decomp.). ^{1}H-NMR (ppm in CD_2Cl_2): 6.65-8.15 (m, aromatic H); ^{31}P-NMR (CD_2Cl_2): 39.6(s), ESI-MS m/z: 662 $[M+H]^+$, Anal. Calcd. for $C_{31}H_{24}Cl_2N_2P_2Pd$: H 3.64, C 56.09, N 4.22; found H 3.67, C 56.50, N 4.18%.

2.2. Suzuki coupling reaction

Typical reaction: A Schlenk flask containing catalyst **2** (24 mg, 0.03 mmol, 1 mol%) was added dry toluene (10 mL). The mixture was degassed by two freeze-thaw cycles. Biphenyl was added as an internal standard followed by K_2CO_3 (1.39 g, 9.12 mmol, 3 equiv.). Chlorobenzene was added using a syringe (340 mg, 3.04 mmol) and in succession, phenylboronic acid (556 mg, 4.55 mmol, 1.5 equiv.) and H_2O (1 ml). The reaction mixtures were heated by oil bath to 110°C and the toluene solution composition analysed using GC.

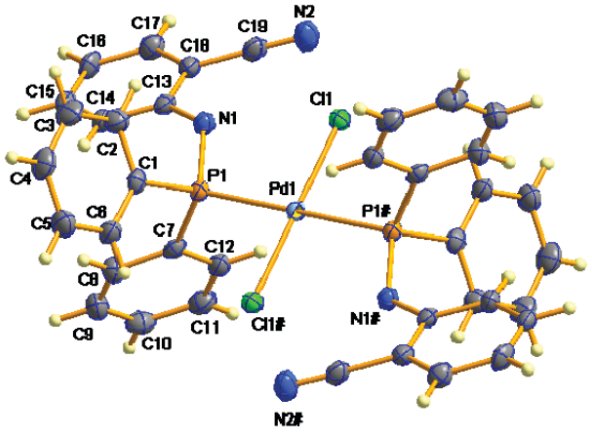


Figure 1. Ortep representation of **2**·2(CH_2Cl_2); atoms are represented by ellipsoids at 50% probability level. Key bond distances (Å) and angles (°) Pd1-Cl1, 2.3195(9); Pd1-P1, 2.3552(9); P1-N1, 1.697(3); P1-C1, 1.827(4); P1-C7, 1.828(4); N1-C13, 1.431(5); C19-N2, 1.152(5); Cl1-Pd1-P1, 93.41(3); Cl1-P1-P1#, 86.59(3); C18-C19-N2, 178.5(4). Demarcated atoms (#) are obtained by the symmetry operation 1-x, -y+1, -z. Dichloromethane solvent molecules omitted for clarity.

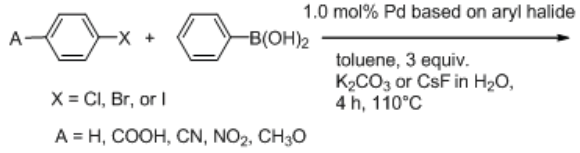
2.3. Structural Characterization in the Solid State

Relevant details about the structure refinements are compiled in Table 2 and selected bond distances and angles given in the captions of Fig. 1. Data collection was performed on a four-circle Kappa goniometer equipped with an Oxford Diffraction KM4 Sapphire CCD at 140(2) K and data reduction was performed using CrysAlis RED. Structure solution and refinement was performed using SHELXTL software package. The structure was solved by Direct methods, followed by full-matrix least-squares refinement (against F^2) with all non-hydrogen atoms refined anisotropically. Hydrogen atoms were placed in their geometrically generated positions and refined using the riding model. Disorder for the solvated dichloromethane molecule was modelled. Empirical absorption corrections (DELABS) were applied. Graphical representations of the structures were made with Diamond.

2.4. TEM sample preparation and TEM analysis

The catalyst solution was diluted with dichloromethane and the NPs separated by centrifugation. The separated NP powders were re-dispersed in methanol. Specimens for TEM were prepared by depositing a drop of this NP dispersion on a carbon coated copper grid (400 meshes). The copper grid was then dried at ambient temperature. A PHILIPS CM20 Transmission Electron Microscope was used and the EDX data were collected on a Thermo Noran System Six X-ray Microanalysis

Table 1. Suzuki cross-coupling reaction in toluene catalyzed by palladium complexes.



Entry	X	A	Base	Yield (%)[a]
1	I	H	K_2CO_3	>99
2	Br	H	K_2CO_3	86
3	Cl	H	K_2CO_3	5
4	I	H	CsF	>99
5	Br	H	CsF	87
6	Cl	H	CsF	4
7	I	COOH	K_2CO_3	>99
8	Br	COOH	K_2CO_3	88
9	Cl	COOH	K_2CO_3	10
10	I	COOH	CsF	>99
11	Br	COOH	CsF	88
12	Cl	COOH	CsF	9
13	I	CN	K_2CO_3	>99
14	Br	CN	K_2CO_3	95
15	Cl	CN	K_2CO_3	6
16	I	NO_2	K_2CO_3	>99
17	Br	NO_2	K_2CO_3	97
18	Cl	NO_3	K_2CO_3	7
19	I	OCH_3	K_2CO_3	92
20	Br	OCH_3	K_2CO_3	10
21	Cl	OCH_3	K_2CO_3	<1
22[b]	I	H	K_2CO_3	>99

[a] Yield determined by GC; [b] $Pd(CH_3CN)_2Cl_2$ containing the same mole of Pd content is used as catalyst

system combined with the CM20 TEM. The calculation of nanoparticle size distribution was based on 200 nanoparticles.

3. Results and discussion

The aminophosphine **1** was prepared according to the literature method [32], with complexes **2** being obtained in quantitative yield by reacting two molar equivalents of **1** with one molar equivalent of $Pd(cod)Cl_2$. Complex **2**, which crystallizes from the reaction mixture as colorless microcrystals, was insoluble in common organic solvents such as dichloromethane, chloroform, tetrahydrofuran and diethyl ether.

The ^1H NMR spectrum of **2** exhibits overlapping aromatic resonances for the protons on the phenyl rings

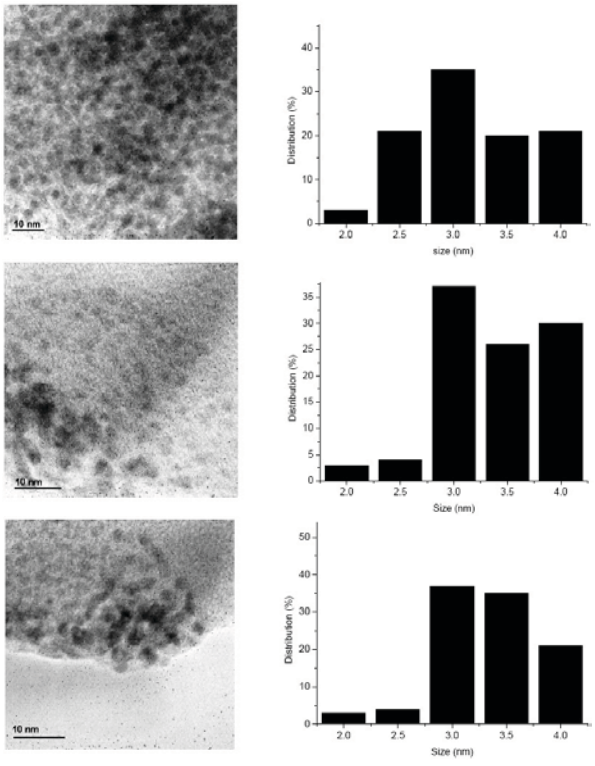


Figure 2. TEM image of palladium nanoparticles separated after Suzuki reaction. (Above: Specimen prepared from Entry 1 of Table 1; Middle: Entry 2; Below: Entry 4).

with the protons on the aniline ring. The chemical shifts for the complexes of **2** in the ^{31}P NMR lie at 39.6 ppm and 32.8 ppm respectively, which are shifted slightly to a higher frequency compared to that of the free ligand **1** (29.0 ppm in d_2-dichloromathene).

Single crystals suitable for X-ray crystallographic analysis were obtained via vapour diffusion of diethyl ether into a solution of the complex **2** in dichloromethane. The structure of **2** is shown in Fig. 1 and key bond parameters are given in the caption. The Pd centre is square-planar with the chloride and aminophosphine ligands disposed *trans*- with respect to each other. The crystal packing is characterised by extensive π–π stacking interactions between phenyl rings of adjacent Pd complexes, and short contacts with cyano- moieties and the dichloromethane solvent molecules. The P-N bond distance 1.697(3) Å is comparable to that of other transition metal (eg. Ni, W, Ru, Pt) aminophosphine complexes [33].

The Suzuki reaction has been attracting intense interest as it is one of the most important synthetic routes for the preparation of asymmetric biaryl building blocks [34]. Palladium(II) complexes such as $Pd(OAc)_2$ and $PdCl_2$ have been used as precatalysts in Suzuki reactions, to yield the catalytically active Pd(0) species

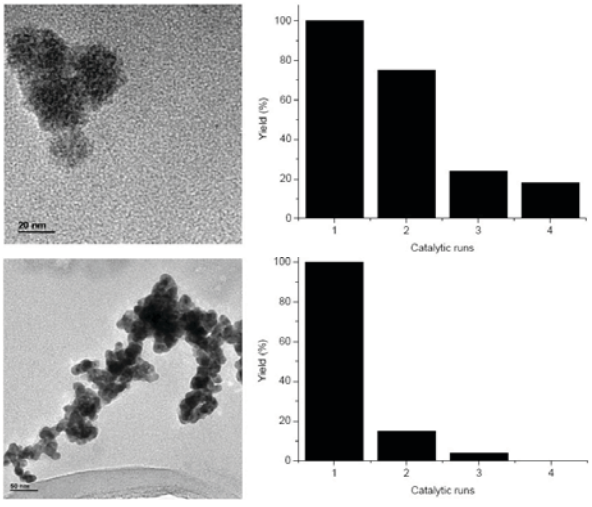
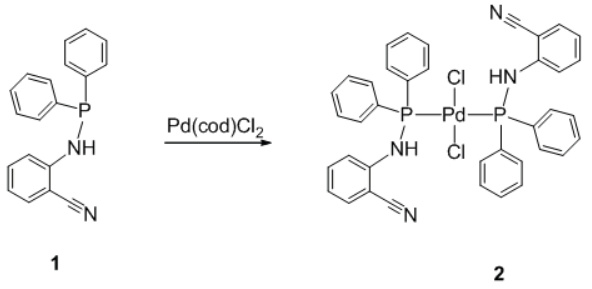


Figure 3. Catalytic system recycling using iodobenzene as substrate and TEM image of Pd NPs taken from the fourth run (Above: Complex **2** as catalyst precursor; Below: $Pd(CH_3CN)_2Cl_2$ as catalyst precursor).



Scheme 1. Synthesis of the complexes **2** and **3**.

[35]. Compound **2** was tested in a standard Suzuki reaction for biphenyl synthesis, and the results from these experiments are summarized in Table 1.

From Table 1 it is evident that the complex is an active catalyst for Suzuki cross-coupling of a range of aryl halides with phenyl boronic acid in toluene. The product yields are dependant on the type of halide of aryl halides. Iodobenzene can be quantitatively converted to biphenyl using K_2CO_3 or CsF as a base. High activities were also observed with bromobenzene (c. a. yield >86%). The substitution group on the aryl halides has also an influence on the reaction results. Those with π-deficient functionalities such as COOH, CN, NO_2 give positive effect on the cross-coupling conversion whereas the electron pushing group OCH_3 offers negative impact (Entry 19, 20, and 21 of Table 1). It is believe that the π-deficient group favours the oxidative addition step of the whole catalytic pathway [36]. However, poor yields were obtained if chlorobenzene derivatives were used as the substrate. It was found that the base used (K_2CO_3 *vs.* CsF) had a minimal impact on catalytic activities. It was also observed that water was needed to generate the active catalyst and subsequently it was found palladium

Table 2. Crystallographic data for of **2**·2(CH2Cl2).

Chem formula	$C_{40}H_{32}Cl_6N_4P_2Pd$
Fw	949.74
Crystal system	Monoclinic
Space group	$P2_1/n$
A (Å)	9.5396(12
B (Å)	13.8165(13)
C (Å)	16.0813(16)
α°	90
β°	92.251(9)
γ°	90
Volume (Å3)	2117.9(4)
Z	2
Dcalc (g cm-3)	1.489
F(000)	926
μ(mm-1)	0.926
Temp (K)	140(2)
Wavelength (Å)	0.71073
Measured reflns	12031
Unique reflns	3669
Unique reflns [I>2σ(I)]	2787
No. of data/restraints/parameters	3669 / 0 / 260
R[a] [I>2σ(I)]	0.0399
wR2[a] (all data)	0.1028
GooF[b]	0.995

[a] $R=\Sigma||F_o|-|F_c||/\Sigma|F_o|$, $wR2=\{\Sigma[w(F_o^2-F_c^2)2]/\Sigma[w(F_o^2)2]\}^{1/2}$
[b] $GooF=\{\Sigma[w(F_o^2-F_c^2)2]/\Sigma n-p\Sigma\}^{1/2}$ *where n is the number of data and p is the number of parameters refined.*

nanoparticles formed during the reaction. Without water, the system proved to be inactive.

Transition-metal nanoparticles are believed to be either the catalyst or catalyst reservoir in many catalytic systems [37-40]. The palladium nanoparticles generated from our reaction systems were isolated and analysed by transmission electron microscopy (TEM) (see Fig. 2). The palladium nanoparticles are observed to be well-dispersed and have an average size ca. 3 – 4 nm.

The catalytic system for Entry 1 was recycled through multiple runs to determine the efficiency of conducting repeated catalyses using the same reaction system. A control test using $Pd(CH_3CN)_2Cl_2$ as a catalyst precursor was also investigated. The yield of the biphenyl product using **2** as a catalyst decreased with increasing recycling with yields dropping below 20% after the fourth run, whereas compared to the $Pd(CH_3CN)_2Cl_2$ system, product yields diminished down below 20% by the 2nd run and the catalyst was completely inactive after the fourth run. The palladium nanoparticles separated from the final cycle were analyzed by TEM (see Fig. 3). It was found that the nanoparticles aggregate into

larger particles (> 100 nm), thereby reducing the active palladium surface available for catalysis. However, it is reasonable to conclude that the ligand **1** exerts a stabilization effect on the palladium nanoparticles since without its existence, huge metallic palladium particles form immediately after the first catalytic run. This observation was consistent with the declining efficiency of the catalytic system, thereby affirming the catalytic role of the palladium nanoparticles in the system. Consequently, alternative methods to stabilize the nanoparticle catalyst, for example, using polyaniline as a support [41,42], and a polymer stabilizer [43], are being considered in our research to improve the catalyst's recycling performance. Nanoparticles from the reaction media were isolated and analyzed using TEM and the results suggests that elemental palladium nanoparticles are important in the catalytic system.

4. Conclusions

A palladium complex comprising a functionalized aminophosphine has been prepared and investigated for catalytic activity in a C-C coupling Suzuki reaction.

Acknowledgements

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